## REMARKS

### Status of the Claims

Claims 1-14 and 17-35 are currently pending. In the present Response, claims 1, 17, 27, and 33 are amended; and new claims 36 and 37 are added. Thus, after entry of these amendments, claims 1-14 and 17-37 are presented for reconsideration.

Pursuant to the Office Action, claims 17-24 and 35 are rejected under 35 U.S.C. §112, first paragraph. Claims 17-24, 31, 33, and 35 are rejected under 35 U.S.C. §112; second paragraph. Claims 1-3, 13, 14, and 25-34 are rejected under the judicially created doctrine of obviousness-type double patenting over U.S. Patent No. 6,268,188.

Applicants respectfully traverse all objections and rejections of the claims.

### Support for the Claim Amendments

Applicants respectfully request entry of the amendments set forth in this response under 37 CFR §1.116. The amendments place the case in condition for allowance and place the case in better condition for appeal; the amendments do not raise any issues of new matter; and, the amended and new claims do not present new issues requiring further consideration or search.

For example, new claims 36 and 37 are directed to nucleic probes that are encompassed by the nucleic probes of claim 17. Claim 36 has the limitation that the nucleic acid sequence be capable of hybridizing under stringent conditions to the polynucleotide sequences that encode the amino acid sequence of SEQ ID NOS:25-32. Nucleic acids capable of hybrizing under stringent conditions would be encompassed by a claim directed to nucleic acids capable of hybridizing under the "mild conditions" of claim 17 as stated in the Office Action. Similarly, claim 37 recites probes having sequences that are complementary or identical to the polynucleotide sequences that encode amino acid sequences of SEQ ID NOS:25-32. Thus, the new claims do not present new issues requiring further consideration or search. Support for new claims 36 and

37 can be found, *inter alia,* at page 3, lines 16-18; page 9, lines 9-13; and page 11, line16-26; and page 12, lines 19-22

The specification has been amended to correct typographical errors. Support for the reference to "*Aquifex* Histidinol-phosphate Aminotransferase" can be found at least at page 5, lines 2-3 of the specification.

Claims 1, 17, 27, and 33 have been amended to correct minor typographical errors and omissions. Support for amended claim 17 directed to a nucleic acid probe which hybridizes to a nucleic acid encoding an enzyme with aminotransferase activity can be found at least at page 11, lines 16-18.

Applicants submit that no new matter has been introduced by the present amendment.

**Objections to the Claims**

Claim 1 has been objected to for missing the phrase "the group consisting of" at the end of line 1. Claim 27 has been objected to for a typographical error.

Applicants submit that the present amendment overcomes these objections.

**Issues under 35 U.S.C. §112, first paragraph**

Claims 17-24 and 35 remain rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, as explained in the Office Action mailed July 6, 2002. Claims 17-24 and 35 also remain rejected under 35 U.S.C. §112, first paragraph, for allegedly not reasonably providing enablement for a probe of 10-50 nucleotides that are 70% complementary to a polynucleotide encoding SEQ ID NOs:25-32, as explained in the Office Action mailed July 6, 2002.

The Patent Office, in its response to Applicants' arguments filed January 10, 2002, states on pages 5 and 6 of the Office Action, "[that the function of the claimed probe is as a probe] is not persuasive because every oligonucleotide can function as a probe, such definition does not distinguish the claimed probes from others in the same class. The specificity can distinguish it but it is not claimed. Regarding enablement, if the probe is not specific, it will hybridize to many functionally and structurally different DNAs."

Applicants have amended claim 17 to provide a specific function for the claimed probes, *i.e.*, the function is that the probes are capable of hybridizing under the stated conditions to a nucleic acid encoding an enzyme having aminotransferase activity. As for enablement, amended claim 17 limits the claimed probes to only those that can hybridize, under the stated conditions, to a polynucleotide that encodes an enzyme having aminotransferase activity. It is within the knowledge of one skilled in the art to design probes, based upon the teaching of the sequences in the instant application, that will hybridize to nucleic acids that encode for enzymes having aminotransferase activity, such as those provided in the specification (*e.g.*, SEQ ID NOS:17-24).

With respect to the written description and enablement rejections to claims 17-24, raised in the July 6, 2001, Office Action, Applicants respectfully submit that amended claim 17 overcomes these rejections. On page 4, of the July 6$^{th}$ Office Action, the Patent Office acknowledges that the claims "impart a structural limitation (70, 90 or 95%)." The Patent Office, however, alleges that "it is unpredictable what function would be encoded by a DNA that hybridizes under mild conditions recited in claim 17 . . . probes would hybridize to DNAs encoding many functionally and structurally unrelated proteins." Applicants respectfully submit that amended claim 17 is directed to probes that hybridize to polynucleotides that encode a polypeptide that must have aminotransferase activity. Accordingly, amended claim 17 includes a functional limitation.

Moreover, Applicants respectfully submit that the specification does enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. In the instant application, Applicants have disclosed the amino acid sequence (*i.e.*, structure) of novel polypeptides having aminotransferase

activity. It should be mentioned that at the time the instant application was filed, the state of the art and level of skill of the artisan in the field of molecular biology was very advanced. Thus, armed with the disclosure provided in the application, one of ordinary skill in the art can use well-known laboratory techniques to make probes that are at least 70% complementary to nucleic acid targets. With these probes, one skilled in the art can screen libraries, use them for diagnostic purposes, or as PCR primers (see, page 8, lines 3-11; page 11, lines 16, to page 12, line 2; and page 12, lines 19-25).

Accordingly, based on Applicants' disclosure, the claimed invention is properly enabled for one skilled in the art to practice the invention. The Patent Office has alleged that this is undue experimentation. Applicants respectfully aver, however, that it would be a matter of routine experimentation, not undue experimentation, for one skilled in the art.

Regarding undue experimentation, the Federal Circuit in *In re Wands* directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" is set forth by the Federal Circuit in, *e.g.*, *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*[1] An applicant had claims that were generic to all IgM antibodies directed to a specific antigen. However, only a single antibody producing cell line had been deposited.[2] The PTO had rejected claims that were generic to all antibodies directed to the antigen as lacking an enabling disclosure.

The Federal Circuit reversed, noting that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited

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1 *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

2 The cell line was a hybridoma, thus, all of the antibodies it produced had the same structure and activity.

to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody species was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of molecular biology for the instant invention also recognize that many constructs may need to be created/isolated and analyzed to isolate the claimed polynucleotides. However, the procedures for making nucleic probes having 70% identity/complementary to a nucleic acid sequence that encodes a polypeptide having aminotransferase activity and, further, utilizing those probes to hybridize to a nucleic acid sequence encoding a polypeptide having aminotransferase activity are widely accepted, routine protocols, not requiring "undue experimentation" to be practiced. Accordingly, one skilled in the art has sufficient guidance by the specification to practice the claimed methods without undue experimentation.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection based upon 35 U.S.C.§112, first paragraph, as applied to claims 17-24 and 35.

**Issues under 35 U.S.C. §112, second paragraph**

Claims 17-24, 31, 33, and 35 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Patent Office alleges that claim 17, drawn to a probe of about 10 to 50 nucleotides, is confusing as the definition in the specification indicates that probes have "at least 10" nucleotides. To further prosecution of the present application, Applicants have amended claim 17 to recite probes having "at least 10 to about 50 nucleotides." It is noted, however, that in the paragraph on page 11, last paragraph, it is stated that probes preferably have at least 10 bases. It does not state that probes must have at least 10 bases.

The Patent Office alleges that claims 18-24 and 35 are rejected as dependent from claim 17. Applicants submit that amended claim 17 is allowable; therefore, dependent claims 18-24 and 35 are allowable as well.

The Patent Office alleges that claim 31 is unclear as reciting "histidinol-phosphate aminotransferase" while the specification recites both "histidinol-phosphate aminotransferase" and "histadine-phosphate aminotransferase." Applicants have amended the specification to correct the typographical error amending "histadine-phosphate aminotransferase" to "histidinol-phosphate aminotransferase."

The Patent Office alleges that claim 33 is unclear as reciting "aminotransferases" activity. Applicants have amended claim 33 to recite "aminotransferase" activity and to also correct additional typographical errors.

**Issues regarding Double Patenting**

Claims 1-3, 13, 14, and 25-34 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over the claims of U.S. Patent No. 6,268,188. Applicants herewith submit the appropriate terminal disclaimer, thus obviating this rejection.

**Allowable Subject Matter**

Applicants thank the Examiner for recognizing that claims 4-12 contain allowable subject matter and that they are objected to only for being dependent upon a rejected base claim and would be allowable if rewritten in independent form. Applicants submit that with the filing of the terminal disclaimer, the base claim is now patentable. Accordingly, claims 4-12 are patentable as well.

CONCLUSION

Claims 1-14 and 17-35 are pending in the application. Claims 1, 17, 27, and 33 have been amended, and claims 36 and 37 are added by the present Response. Applicants request that

the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants believe that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

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**Version with markings to show changes made**

In the specification:

Paragraph beginning at page 26, line 25 has been amended as follows:

***Aquifex* [Histadine] Histidinol-phosphate Aminotransferase**

In the claims:

Claims 1, 17, 27, and 33 have been amended as follows:

1. (Thrice Amended) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide encoding an enzyme with aminotransferase activity wherein the amino acid sequence of the enzyme is at least 70% identical to SEQ ID NOS:25-32; and

b) a polynucleotide comprising a nucleic acid sequence complementary to a polynucleotide of a).

17. (Twice Amended) A nucleic probe comprising a nucleic acid sequence wherein the nucleic acid sequence consists of an oligonucleotide from at least [about] 10 to about 50 nucleotides in length and having a region of nucleotides that is at least 70% complementary to a nucleic acid target region of a nucleic acid encoding an amino acid sequence selected from the group consisting of SEQ ID NOS:25-32 and which hybridizes to a [the] nucleic acid target region of a nucleic acid encoding an enzyme with aminotransferase activity to form a detectable target:probe duplex under conditions that include 0.9 M NaCl, 5.0 mM $NaH_2PO_4$, 5.0 mM $Na_2$ EDTA, 0.5% SDS and 10X Denhardt's at about 45°C.

27. (Amended) The polynucleotide of claim 2 which encodes an adenosyl-8-amino-7-oxononanoate aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:27.

33. (Amended) An isolated polypeptide encoding an enzyme with aminotransferase[s] activity, wherein the polynucleotide[s] encodes the enzyme of SEQ ID NO[S]:25, SEQ ID

NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, or SEQ ID NO:32.